REMARKS

Claim 1 was pending in the application. Claim 1 has been amended to more fully and distinctly claim the present invention. New claims 32-46 have also been added. Accordingly, claims 1 and 32-46 are currently pending in the present application. Support for amended claim 1 may be found in the instant specification at least, for example, at page 16, line 24 through page 18, line 39 and page 39, lines 24-29. Support for added claims 32-40 may be found in the instant specification at least, for example, at page 17, line 9 through page 18, line 39, page 31, lines 13-34 and page 39, lines 24-29. No new matter has been added.

Attached hereto is Appendix A, captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**" The attached Appendix includes a marked-up version of the changes made to the claims by the current amendment. Also attached hereto is APPENDIX B, which includes the full set of claims that will be pending after entry of the instant amendment.

Amendment to the claims is not to be construed as acquiescence to any of the rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the instant application. Applicants reserve the right to pursue the claims as originally filed, or similar claims, in this or one or more patent applications.

Claim Rejections Under 35 U.S.C. §112, first paragraph

Claim 1 has been rejected under 35 U.S.C.§112, first paragraph for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 has further been rejected under 35 U.S.C. §112, first paragraph, as not reasonably providing enablement for eliciting a response in any T cell by any agent *ex vivo* or *in vivo*.

Specifically, the Examiner states that claim 1 "[e]mbraces a genus of agents that could interact with T cells in many different ways, such as via a cell surface receptor, or via a co-stimulatory signal. However, such agents essential for practice [sic] the invention are only defined by the effects rather than the chemical or physical structures." The Examiner further states that "considering the breadth of the claim, it embraces protecting T cell death using a

genus of agents that could interact with T cells in many different ways *in vitro* and *ex vivo*. However, the specification fails to teach the common attribution of such agents, or how to identify these agents."

Although Applicants traverse this rejection, in an effort to expedite prosecution and without acquiescing to the Examiner's rejection, Applicants have amended claim 1 to include contacting the T cell *ex vivo* with at least two agents selected from the group consisting of an anti-CD28 antibody, an anti-CD3 antibody, an anti-CD2 antibody, a CD28 ligand, interleukin-2 (IL-2), ionomycin, A23187, phorbol-12, 13-dibutyrate, a lectin and a superantigen (see, *e.g.* page 16, line 24 through page 18, line 39). Applicants also teach assays which can be used to identify additional agents within the scope of Applicants claims which can be used to augment Bcl-X_L protein levels in a cell (see page 19, lines 15-22). These assays involve incubating T-cells in the presence or absence of a test agent and determining the amount of Bcl-X_L protein produced by the cell at different times by, for example, Western blot analysis (described, for example, in Examples 4 and 5).

Applicants thus maintain that the specification provides sufficient written description for the amended claims and that one of skill in the art would be enabled to practice the invention without undue experimentation. Accordingly, these rejections have been obviated and Applicants respectfully request that the Examiner withdraw these rejections.

Claim Rejection Under 35 U.S.C. §102

Claim 1 has been rejected under 35 U.S.C. 102(e) as being anticipated by Thompson *et al.* (U.S. 6,303,331). The Examiner states that "Thompson *et al.* teach a method for inhibiting cell death in a cell *in vitro* comprising contacting the intended cells for protection with an effective amount of a polynucleotide encoding a Bcl-X_L polypeptide operably linked to a promoter, whereby expression of said Bcl-X_L polypeptide inhibits programmed cell death of said cell, wherein the cell is a lymphocyte, a CD4 cell." Because a CD4 cell is a T cell, the Examiner concludes that claim 1 is therefore anticipated by Thompson *et al.*

Claim 1 has also been rejected under 35 U.S.C. §102(f) because the applicant did not invent the claimed subject matter. Specifically, the Examiner states that "the application has a different inventive entity with a single common inventor as that of U.S. Patent 6,303,331.

Because claim 1 of the instant application is anticipated by the claims 1, 7, and 8 of the cited patent, the inventive entity on the instant application appears to be unclear with regards who is the real inventor."

Applicants respectfully traverse and as stated above, in an effort to expedite prosecution and in no way acquiescing to the Examiner's rejection, have amended claim 1 to refer to agents which do not include a polynucleotide encoding Bcl-X_L polypeptide. Accordingly, the rejection is rendered moot by the present amendment and Applicants therefore request withdrawal of this rejection.

Claim Rejection Under 35 U.S.C. §103

Claim 1 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Boise *et al.* and in view of Choi *et al.* Specifically, the Examiner states that Boise *et al.* teach contacting a plasmid encoding human Bcl-X_L or bcl-2 or both, with an IL-3-dependent cell line, and then observing cell survival after IL-3 deprivation. The Examiner further states that "although Boise *et al.* do not teach contacting T cells with Bcl-X_L vector in the reported experiments, it would have been obvious to one of ordinary skill in the art seeking to improve T cell survival, at the time the invention was made, to modify the methods taught by Boise *et al.* by simply substituting the IL-3-dependent cells with T cells with a reasonable expectation of success."

Applicants respectfully traverse. To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under 35 U.S.C. §103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in Applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1529, 1531 (Fed. Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, *e.g.*, *Carella v. Starlight Archery*, 804 F.2d 135, 231,

USPQ 644 (Fed. Cir. 1986), and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985).

Applicants submit that the Examiner has failed to establish a prima facie case of obviousness, since the cited references alone or in combination, fail to provide the necessary motivation for the ordinarily skilled artisan to combine the methods taught by Boise *et al.* with the teachings of Choi *et al.*

Moreover, even if one were to combine the references as suggested by the Examiner, neither reference alone or in combination teach the claimed invention. Boise, *et al.* teach that stably transfecting a nucleic acid encoding a Bcl-X_L protein into an IL-3-dependent cell line will inhibit cell death upon growth factor withdrawal at least as well as bcl-2. However, there is no suggestion or motivation to use agents such as anti-CD28 antibody, an anti-CD3 antibody, an anti-CD2 antibody, a CD28 ligand, interleukin-2 (IL-2), ionomycin, A23187, phorbol-12, 13-dibutyrate, a lectin and a superantigen to augment Bcl-X_L protein levels.

Chio *et al.* teach that ligation of CD40 induces the appearance of Bcl-X_L protein in WEHI-231 cells (an immature B cell lymphoma cell line), thereby protecting these cells from anti-IgM-mediated apoptosis. This reference, however, fails to teach or suggest the role of Bcl-X_L in T cells, as required by Applicants claims. Since CD40 is a B-cell specific co-stimulatory molecule, an ordinarily skilled artisan reading the teachings of Chio *et al.* would not have been motivated to apply the teachings of Chio *et al.* in T cells. Moreover, Choi *et al.* fails to teach the elements missing from Boise, *et al*, namely to use agents such as an anti-CD28 antibody, an anti-CD3 antibody, an anti-CD2 antibody, a CD28 ligand, interleukin-2 (IL-2), ionomycin, A23187, phorbol-12, 13-dibutyrate, a lectin and a superantigen to augment Bcl-X_L protein levels, as claimed.

In view of the above, it is Applicants' position that (1) the Examiner has failed to establish a prima facia face of obviousness and (2) the references relied upon by the Examiner either alone or in combination, fail to teach or suggest the claimed invention.

Double Patenting

Claim 1 has been rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1, 7 and 8 of U.S. Patent No. 6,303,331 and claims 1

and 3 of U.S. Patent No. 6,143,291. As amended, claim 1 is patentably distinct from claims 1, 7 and 8 of U.S. Patent No. 6,303,331 and claims 1 and 3 of U.S. Patent No. 6,143,291. Accordingly, these rejections are rendered moot by the present amendment.

CONCLUSION

If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP

DeAnn F. Smith
Reg. No. 36,683
Attorney for Applicant

Dated: **June 6, 2002**

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim 1 has been amended as follows:

1. (Amended) A method for protecting a T cell from cell death, comprising contacting the T cell *ex vivo* with at least two agents selected from the group consisting of an anti-CD28 antibody, an anti-CD3 antibody, an anti-CD2 antibody, a CD28 ligand, interleukin-2 (IL-2), ionomycin, A23187, phorbol-12, 13-dibutyrate, a lectin and a superantigen which augments BCL-X_L protein level in the T cell such that the T cell is protected from cell death.